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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)
MAY 80 A W SINGER
USAEHA-75-51-0901-80

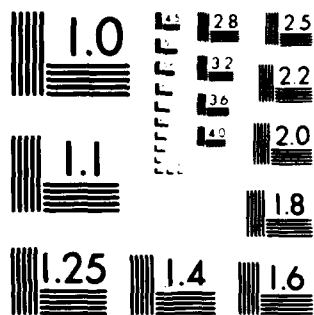
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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36469
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND
STUDY NO. 75-51-0901-80
MAY 1976-MARCH 1980

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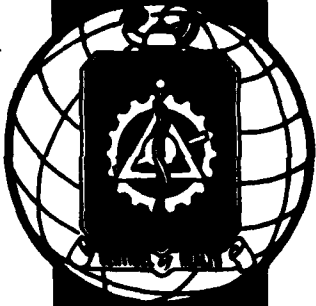
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7. AUTHOR(s) ALLEN W. SINGER CPT, VC		6. PERFORMING ORG. REPORT NUMBER										
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19. KEY WORDS (Continue on reverse side if necessary and identify by block number) <table border="0"><tr><td>AI3-36469</td><td>Topical Hazard Evaluation</td></tr><tr><td>Candidate Repellent</td><td>USDA Proprietary Compound</td></tr><tr><td>Guinea Pig Sensitizer</td><td>Acute Ingestion Hazard</td></tr><tr><td>Eye Irritation</td><td>Photoactivated Skin</td></tr><tr><td>Skin Irritation</td><td></td></tr></table>			AI3-36469	Topical Hazard Evaluation	Candidate Repellent	USDA Proprietary Compound	Guinea Pig Sensitizer	Acute Ingestion Hazard	Eye Irritation	Photoactivated Skin	Skin Irritation	
AI3-36469	Topical Hazard Evaluation											
Candidate Repellent	USDA Proprietary Compound											
Guinea Pig Sensitizer	Acute Ingestion Hazard											
Eye Irritation	Photoactivated Skin											
Skin Irritation												
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) A preliminary hazard evaluation of AI3-36469 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound did not cause direct or photoactivated skin irritation, nor eye irritation, and was not acutely toxic by ingestion. It did, however, sensitize two of nine guinea pigs. This potential for human skin sensitization resulted in a recommendation to disapprove further testing with this candidate insect repellent.												

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U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

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HSE-LT-T/WP

21 MAY 1980

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent
AI3-36469, US Department of Agriculture Proprietary Compound, Study
No. 75-51-0901-80, May 1976 to March 1980

Executive Secretary
Armed Forces Pest Management Board
Forest Glen Section, WRAMC
Washington, DC 20012

A summary of the pertinent findings and recommendations of the inclosed report follows:

A preliminary hazard evaluation of AI3-36469 was performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compound did not cause direct or photoactivated skin irritation, nor eye irritation, and was not acutely toxic by ingestion. It did, however, sensitize two of nine guinea pigs. This potential for human skin sensitization resulted in a recommendation to disapprove further testing with this candidate insect repellent.

FOR THE COMMANDER:

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U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

HSE-LT-T/WP

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36469
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND
STUDY NO. 75-51-0901-80
MAY 1976-MARCH 1980

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, Florida, 5 May 1976.

b. Memorandum of Understanding between the US Army Environmental Hygiene Agency, the US Army Health Services Command; the Department of the Army Office of The Surgeon General, the Armed Forces Pest Control Board; and the US Department of Agriculture, Agricultural Research, Science and Education Administrations, titled, Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCE. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), 1972, revised 1976.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-36469.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-36469, US Department of Agriculture (USDA) Proprietary Compound, was conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows: *†

* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication No. (NIH) 74-23, revised 1978.

† The experiments reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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Study No. 75-51-0901-80, May 76-Mar 80

TABLE. PRESENTATION OF DATA

Test	Results	Interpretation
<u>SKIN IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	Compound AI3-36469 did not cause any irritation of the intact skin or of the skin surrounding an abrasion.	USAEHA Category I (ref Appendix).
0.5 mL technical grade compound applied to each of six rabbits.		
<u>EYE IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hour application of 0.1 mL technical grade compound to one eye of each of six New Zealand White rabbits.	Compound AI3-36469 did not cause any irritation to the cornea or conjunctiva of any rabbit tested.	USAEHA Category A (ref Appendix).
<u>APPROXIMATE LETHAL DOSE (ALD)</u>		
<u>Oral</u>		
Rats (male) - no diluent	ALD = 4900 mg/kg	Presents little lethal hazard from accidental ingestion.

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Test	Results	Interpretation
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PHOTOCHEMICAL SKIN IRRITATION STUDIES

Rabbits

A single 0.05 mL application of a 25 percent (w/v) solution of the compound and a 10 percent (w/v) Oil of Bergamot solution (positive control) in 95 percent ethyl alcohol were applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes at a distance of 10-15 cm.

A 25 percent solution of AI3-36469 in ethanol did not cause a photochemical irritation reaction under test conditions.

Compound AI3-36469 did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irritation in humans.

Control

Following UV exposures of the rabbits, 0.05 mL of test compound, positive control and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation at 24, 48 and 72 hours.

Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.

Study No. 75-51-0901-80, May 76-Mar 80

Test	Results	Interpretation
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SENSITIZATION STUDIES

Guinea Pigs (Male)

Intradermal injections of 0.1 mL of a 0.1 percent solution (w/v) of AI3-36469 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.

Ten test guinea pigs were given 10 sensitizing doses over a 3-week period. After 2 weeks rest, they were challenged with ID injections of test compound.

Ten positive control guinea pigs were sensitized over 3 weeks with DNCB. After 2 weeks rest, they were challenged with ID injections of DNCB.

Challenge dose of AI3-36469 produced a sensitization reaction in two of nine guinea pigs.

Challenge dose of DNCB in positive control guinea pigs produced a marked sensitization reaction in 10 out of 10 guinea pigs.

Compound AI3-36469 produced a mild sensitizing reaction in two guinea pigs, indicating potential exists for human skin sensitization.

DNCB produced a marked reaction, indicating the guinea pigs respond to sensitizing agents.

* A known skin sensitizer

Study No. 75-51-0901-80, May 76-Mar 80

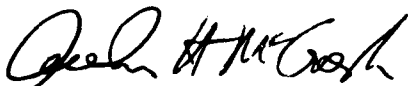
5. CONCLUSION. Technical grade compound AI3-36469 caused a mild sensitizing reaction in two of nine guinea pigs and, hence, the potential for human sensitization exists.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-36469, USDA Proprietary Compound, not be approved for further testing as a candidate insect repellent.



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Veterinary Animal Laboratory Officer
Toxicology Division

APPROVED:



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Chief, Toxicology Division

APPENDIX

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals. prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.